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Javier Escudero, *Member, IEEE*, Antonio Ibáñez-Molina, and Sergio Iglesias-Parro

***Abstract*—Cognitive functions result from the interplay of distributed brain areas operating in large-scale networks. These networks can be modelled with a number of parameters that represent their underlying dynamics. One particularly fruitful model to simulate key aspects of the large-scale brain networks is the Kuramoto model, which simulates the phase evolution of several weakly coupled oscillators that represent the mean oscillatory behavior of different cortical regions. Here, we inspected the dependency of two widespread nonlinear complexity markers, Sample Entropy (*SampEn*) and Lempel-Ziv Complexity (*LZC*), on EEG activity generated with a Kuramoto phase model where the time delay and connectivity strength among oscillators varied. We also added different levels of noise to the electroencephalogram (EEG) signals. Our results indicated that both complexity metrics reflected the changes in the delays and global synchrony levels, but we found that *SampEn* was slightly more sensitive to the state transition and its results were less affected by the presence of noise. These results help in the effort to understand the dynamics of EEG recordings and their relationship to large-scale networks.**

I. Introduction

It has long been proposed that cognition results from the dynamical interactions of distributed brain areas operating in large-scale networks [1]. Yet, the specific nature of this complex interaction remains unclear. Phase synchronization between oscillators has been studied widely as a potential mechanism for reciprocal interaction. According to this point of view, complex cognitive functions emerge from a balanced interplay between integrating and segregating influences that operates in a metastable dynamic regime [2].

The concepts of complexity and synchrony are central in the effort to understand the structural dynamics of electroencephalogram (EEG) recordings and their relationship to cognitive functions. Although early studies suggested that EEG complexity, as measured by correlation dimension (D_2), was independent of the interaction between distant cortical generators [3], recent emphasis on brain connectivity has proven that, indeed, long range synchronization is a key element of brain function. Hence, in order to understand the emergence of different patterns of EEG complexity (or structural irregularity measured with non-linear estimators), we need to study how it relates to long-range cortical synchronization. One approach to do so is to model different states of synchrony between large-scale neural generators. In this type of models, the modulation of physiologically meaningful parameters affects the generated brain activity through the level of synchrony in the model.

A seminal study [4] proposed a mean-field model of nearly identical weakly coupled oscillators. It showed that, at low levels of coupling with each oscillator running at its natural frequency, the system behaves incoherently [4]. However, when coupling strength exceeds a certain threshold, a small cluster of oscillators become locked in phase and amplitude [4]. Based on [4], Kuramoto proposed an exactly solvable phase model and showed that the system sometimes synchronizes despite differences in the natural frequencies of the single nodes [5]. The Kuramoto model has successfully been used to simulate EEGs [6].

A recent study has evaluated the mechanisms of spontaneous magnetoencephalogram (MEG) functional connectivity using the Kuramoto model of coupled oscillators together with realistic whole brain structural and physiological information [7]. The results of this study supported the choice of the Kuramoto model and indicated that the structured amplitude envelope fluctuations observed in resting-state MEG recordings may originate from spontaneous synchronization mechanisms naturally occurring in the space-time structure of the brain sources [7].

However, the impact of the model's parameters in the complexity of brain signals has not been inspected yet, even though the field of non-linear analysis has been fruitful in EEG characterization [8], [9]. This is probably due to two main reasons. First, complexity estimations may depend on a wide range of signal characteristics and it is not always clear which one is leading a particular change [10]. Second, several alternative definitions of non-linear complexity are available in the literature [11]. For example, the commonly used Sample Entropy (*SampEn*) is, in fact, a regularity estimator derived from the signal entropy analysis [12]. An alternative definition of complexity is the Kolmogorov (or algorithmic) complexity, where the complexity of a given sequence of zeros and ones is given by the number of bits of the shortest computer program which can generate it. An example of this kind of complexity measures is the Lempel-Ziv Complexity (*LZC*) [13]. Another alternative is that of dimensional complexity, which is related to the fractal characteristics of the signals [11]. This was traditionally measured with D_2. However, the use of this metric in biomedical data is problematic due to the typical short length of the signals and the presence of noise [8].

Thus, we aim at evaluating how the output of two non-linear complexity (or irregularity) metrics widely used in the analysis of brain signals (*SampEn* and *LZC*) depends on key

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parameters of the Kuramoto model. We expect that these analyses will provide relevant information to untangle the interrelationship between the synchrony and complexity of brain activity, and to understand the similarities and differences of commonly used non-linear metrics.

II. Simulated Electroencephalogram Activity

A. Kuramoto model

Kuramoto showed that for any system of weakly coupled limit-cycle oscillators, the long-term dynamics could be simulated by [5]:

$$\frac{\mathrm{d}\theta_i}{\mathrm{dt}} = \omega_i + k\sum_{j=1}^{N} C_{ij}\sin\left(\theta_j\left(t-\tau_{ij}\right)-\theta_i(t)\right), \quad i=1,\ldots,N$$

where θ_i is the phase of the i^{th} oscillator on its limit cycle and ω_i is its natural frequency ($f_n = \omega_i/2\pi$), drawn from a fixed Gaussian distribution with mean f_0 and standard deviation σ_f (f_0=60Hz and σ_f = 1Hz in our analyses). The term C_{ij} is the relative coupling strength from oscillator i^{th} to oscillator j^{th} (representing the number of fibers between regions and the synaptic weights), and k is the global excitatory coupling strength, a parameter that scales all coupling strengths. τ_{ij} is the structural conduction delay between the i^{th} and j^{th} oscillators.

For the Kuramoto model, synchronization is conveniently measured by an order parameter (r):

$$r(t) = \left| 1/N \sum_{j=1}^{N} e^{i\theta_j} \right|$$

where $0 \le r(t) \le 1$ measures the phase coherence of the N oscillators. If all oscillators are perfectly synchronized with identical angles $\theta_i(t)$, then $r(t) = 1$. In contrast, if all oscillators are spaced equally on the unit circle, then $r(t) = 0$.

B. Implementation of the model

Our model implements 66 Kuramoto oscillators coupled together according to human white matter tractography obtained from [14]. The tractography information is used to determine which region pairs are connected by putative white matter fiber tracts, and to obtain length and fiber density. The length and fiber density serve as the basis for the elaboration of the connection strength (C) and conduction delay (τ) matrices.

Initial conditions correspond with the first 1000 samples (100ms). The model is simulated for 25s using an Euler's integrator scheme with 0.1ms time steps. All simulations start with k=0. After 5×10^3 steps, k is increased by 5×10^{-5} on each time step. Thus, the value of k varies through the simulations, which are repeated 15 times for 3 types of delays. That is, each τ_{ij} is normalized to set the average value of all τ_{ij} ($\bar{\tau}$) to 0.5, 3, and 5.5ms. These values are chosen because they lead to three different levels of synchronization in the model. All calculations are performed using Matlab®.

C. Simulated EEGs for experimentation

EEG activity from 32 sensors is simulated for each model according to the following weighted sum of the activity in each source (oscillator) from the model:

$$x_i(t) = \sum_{j=1}^{N} w_{ij}\sin\left(\theta_j(t)\right) + \varepsilon_i(t), \quad i=1,\ldots,P$$

where $x_i(t)$ is the time series from sensor i, w_{ij} is the weighted contribution of source j in sensor i. Each w_{ij} was calculated using a standard forward model algorithm (BESA 2000) in which the contribution of each oscillator to each sensor was obtained in two steps. First, each oscillator was located in the head model according with its Talairach coordinates and it is then considered a cortical source. Second, the weights of these sources were normalized to a maximum value of one. The term $\varepsilon_i(t)$ represents uncorrelated white Gaussian noise added to the signal. All simulations are repeated for $\varepsilon_i(t) = 0$ (no noise), and noise levels with signal to noise ratio (SNR) of 20, 10 and 0 dBs.

Hence, we conduct a total of 15 (repetitions) × 3 (delay levels) × 4 (noise levels) EEG sets of 25s each one.

III. Complexity Metrics

We consider two commonly used non-linear metrics, each of which represents a slightly different view of the concept of "complexity": *SampEn* and *LZC*.

A. Sample Entropy (SampEn)

SampEn is an irregularity measure defined as a modification of approximate entropy to reduce its bias. *SampEn* computes the negative of the logarithmic conditional probability that sets of patterns which are closer than a tolerance, r, for m contiguous samples will remain similar at the next point (pattern length m+1). *SampEn* excludes self-matches. Higher values of *SampEn* are associated with more irregular data [8], [12].

The values of m and r are critical in the computation of *SampEn* and they should be fixed across comparisons. No strict guidelines exist to facilitate their choice a priori. In this work, we have used values of m=2 and r=0.10 times the standard deviation of the signal, as these are some of the recommended values in the seminal *SampEn* paper [12].

B. Lempel-Ziv Complexity (LZC)

LZC is a widely used metric of complexity in the Kolmogorov's sense [13]. It has been widely applied to biomedical signals [10] and related to signal concepts such as the bandwidth of random processes and the harmonic variability in quasi-periodic signals [10].

LZC is a non-parametric metric that assesses the number of distinct substrings and their rate of recurrence along the time series, assigning higher values to more complex data (higher number of substrings) [10], [13]. It requires the signal to be binarized according to a predefined threshold. In this study, we use the median of the signal.

C. Complexity analysis of the simulated EEGs

SampEn and *LZC* are applied to each channel of the simulated EEG signals, which have been band-pass filtered between 2Hz and 80Hz to replicate the process used to select a typical band of interest in EEG analysis. To account for the

dependency of the complexity measures on the evolution of k, we compute them using a sliding window procedure. Successive epochs of the EEGs are selected with a sliding window of 2s (i.e., 2000 samples, the final sampling frequency is 1kHz). This epoch length is similar to that used in other non-linear analysis of electrophysiological brain signals [8]. The sliding windows have 50% overlap. Finally, the complexity metrics are computed within each window and they are visually inspected to identify potential dependencies on k, $\bar{\tau}$, and the level of noise added to the simulated EEGs.

IV. Results

First, we illustrate how $r(t)$ depends on the values of k and $\bar{\tau}$ in Fig. 1. $r(t)$ measures the overall synchronization of the model averaged across the 15 repetitions, with error bars showing the 95% confidence interval (CI). The level of synchronization increased as the average structural conduction delay decreased (from 5.5ms, to 3ms, and to 0.5ms). The effect of k is most noticeable for τ=3ms, where a sudden increase in synchronization starts happening around k≈6.5. A similar, but less pronounced, effect can be seen for τ=5.5ms when k≈5ms.

We depict the dependency of the non-linear metrics on the levels of $\bar{\tau}$, k and the amount of noise added to the signals in Fig. 2 (*SampEn*) and Fig. 3 (*LZC*). Averages were computed across the 15 independent repetitions of the simulated EEG signals. The figures show the mean of these results across all 32 EEG channels with the bars indicating 95% CI across channels.

The effect of $\bar{\tau}$ was clear for both *SampEn* and *LZC*. High values of $\bar{\tau}$ produced more complex EEG for all levels of k, although it was less evident in conditions with the maximum level of noise (SNR=0dB). Surprisingly, the relationship between k and complexity was not linear. That is, as k increased during simulations, *SampEn* and *LZC* did not necessarily decreased. In fact, for low levels of k, complexity values tended to increase in parallel with this parameter. It is noteworthy that for values of k in the interval $4 \leq k \leq 8$, we usually found a rapid decrease of *SampEn* and *LZC* except for short delays (0.5 ms). Interestingly, this result is stronger for $\bar{\tau}$=3ms, when there is a transition in the stability of global synchrony from a metastable state to a less

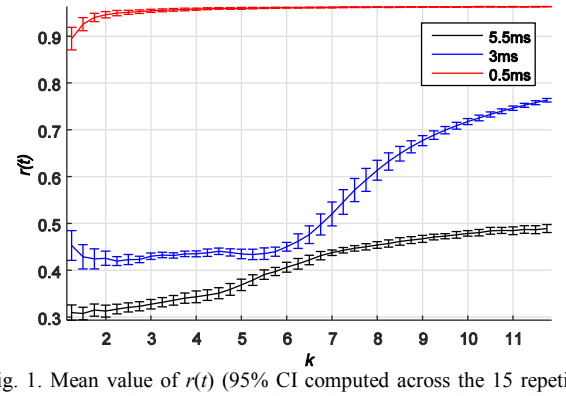

Fig. 1. Mean value of $r(t)$ (95% CI computed across the 15 repetitions shown as error bars) as a function of τ (0.5ms: red; 3ms: blue; and 5.5ms: black) and k (as shown in the abscissa).

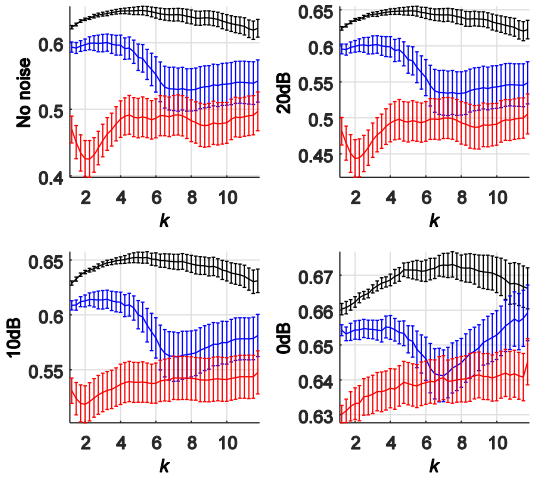

Fig. 2. Mean value of *SampEn* (95% CI shown as error bars) as a function of τ (0.5ms: red; 3ms: blue; and 5.5ms: black), k (as shown in the abscissa), and level of additive noise (top left: no noise; SNR=20dB: top right; SNR=10dB: bottom left; SNR=0dB: bottom right).

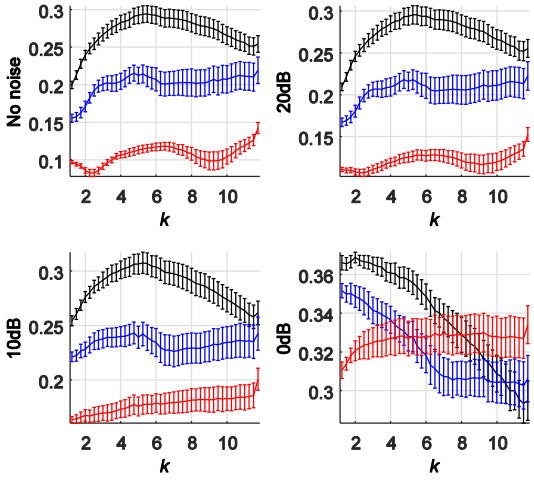

Fig. 3. Mean value of *LZC* (95% CI shown as error bars) as a function of τ, k, and level of additive noise in EEG channels. Format is as in Fig. 2.

variable and more synchronized state (see Fig. 1). Hence, *SampEn* and *LZC* seems to be sensitive to metastable states or transitions in which $r(t)$ exhibit more variability.

Both *SampEn* and *LZC* produced qualitatively similar estimations of complexity indicating that they were equally sensitive to delays and global synchrony levels. However, there was a slight advantage in the case of *SampEn*, as this metric showed more sensitivity to the state transition in synchrony for $\bar{\tau}$=3ms and its values were less distorted in the presence of high level of noise.

V. Discussion and Conclusions

In this study, we have used a set of Kuramoto mean-field models [5]–[7] to explore the role of $\bar{\tau}$ and k in the complexity of the observed EEGs. It had been hypothesized that a more globally synchronized system would produce less irregular behaviors. Hence, we expected a clear negative relationship between the synchrony level of the model – $r(t)$

–, which is modulated by $\bar{\tau}$ and k, and complexity estimations. Overall, our estimations of entropy (*SampEn*) and randomness (*LZC*) of synthetic EEGs tended to show this negative dependency, but it was not straightforward as it depended on specific values of $\bar{\tau}$ and k.

The study of the effect of changes in $\bar{\tau}$ on the Kuramoto phase model is important. This is because, in neural networks, the effect of the synaptic, dendritic, as well as the propagation delays, can be significant. According to [15], the time delay introduces de-phasing among oscillators. The relationship between time delay and phase agreement has been also showed in [16], [17]. Present work provides further evidence on the interplay between delay and phase synchronization. Moreover, we also showed that complexity measures seem to be sensitive to such relationship.

Kuramoto [5] showed that the phase model exhibits a spontaneous transition from incoherence to collective synchronization, as the coupling strength past a certain threshold (k_c). Here, we show a Hopf bifurcation illustrating the transition in the stability of global synchrony from a metastable state to a less variable, synchronized state depending on k values. However, the appearance of this bifurcation seems to depend on the time delay present in the model. The Hopf bifurcation it is only apparent for $\bar{\tau}$ =3ms. Complexity measures seems to respond differently to this interaction between synchrony, and k and τ, with *SampEn* reflecting this change more clearly.

From the point of view of the complexity metrics, several authors [11], [18] have used a concept of complexity based on "meaningful structural richness" in the sense that a system is complex when it has various parts that are linked together, and when the relationships among these parts involve several degrees of coordination. Indeed, this notion of complexity intuitively relates to synchronization between different parts of a system. It implies that complex systems are neither completely regular nor completely random. In this context, a complexity metric should measure off-equilibrium order and, therefore, *SampEn* and *LZC* do not fulfil this criterion. They are, however, widespread tools for biomedical signal analysis that have led to significant results in various settings. Appropriate multiscale extensions of these techniques will probably fulfil this criterion, and major developments have recently been achieved in this direction [18], [19]. Their relationship with synchrony in the light of the Kuramoto model will be subject of future work. It will also be important to fully characterize the robustness of these and other common nonlinear metrics to the presence of noise in the signals, and to evaluate other types of underlying oscillators [20].

To sum up, we inspected the dependency of two widespread nonlinear metrics, *SampEn* and *LZC*, on the values of the global excitatory coupling strength (k) and the structural conduction delay (τ) of a Kuramoto model simulating EEG recordings to understand the relationship between the complexity and synchrony of brain activity. The results indicate that both *SampEn* and *LZC* are sensitive to changes in the delays and global synchrony levels, but we found that *SampEn* was slightly more sensitive to the state transition in synchrony for τ=3ms and its results were less affected by the presence of noise. These preliminary results shed light on the nonlinear dependency between synchronization and complexity metrics for experimental data about brain activity.

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